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EXAMINER
JAMROZ, MARGARET E

ART UNIT	PAPER NUMBER
1644	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/822,110	WANG, HWA-CHAIN ROBERT	
	Examiner	Art Unit	
	Margaret E Jamroz	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/23/01 and 1/23/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,32-37 and 42-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,32-37 and 42-52* is/are rejected.

7)☒ Claim(s) *12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 01/23/02 (Paper No. 11), is acknowledged.

Claims 1-12, 32-37, and 42-52 are pending.

2. Applicant's election without traverse of Group III (claims 1-12, 32,and 42-50, now claims 1-12, 32-37, and 50-52) in Paper No. 10 is acknowledged. Upon further consideration, claims 42-49 have been rejoined with Group III.

Applicant further elected a species of a peptide of SEQ ID NO: 5. However, SEQ ID NO: 5 is now found to be free of prior art. The prior art search has been extended to cover SEQ ID NO: 2, recited in claims 11-12, and SEQ ID NOS: 3-4 and 6-76.

Claims 1-12, 32-37, and 42-52 wherein the compound, compositions thereof, and kit comprising a peptide, SEQ ID NO: 3-76, and a polypeptide consisting essentially of positions 1-322 of SEQ ID NO: 2 and a polypeptide consisting of positions 1-322 of SEQ ID NO: 2 are under consideration in the instant application.

3. The abstract of the disclosure is objected to because it does not describe the claimed invention. Applicant is claiming an isolated peptide and uses thereof, whereas the abstract is drawn to antibodies and uses thereof.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Correction is required. See MPEP § 608.01(b).

4. The title of the invention is not descriptive. A new title is required that is *clearly indicative of the invention to which the claims are directed*.

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP 6.08.01(o). Correction of the following is required:

A labeled isolated peptide, wherein the label is a spin label or chemiluminescent label as recited in claim 48 lacks antecedent basis in the instant specification.

7. The disclosure is objected to because of the following informalities: on page 4, line 1, and page 6, lines 2-3 and 7, applicant discloses peptide SEQ ID NOS: 3-**79**. Applicant has only submitted peptide SEQ ID NOS: 3-**76**. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-10, 32-37, 44-45, 47, and 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 1-6 are indefinite and ambiguous in the recitation of "about 20/30/40/50/60/70 amino acids". On skilled in the art could not determine how long the amino acid sequence should be, or if it should be the exact number of residues as recited.

11. Claims 1-10 are indefinite and ambiguous in the recitation of "at least a first contiguous amino acid sequence" and "at least a second contiguous amino acid sequence". One skilled in the art could not determine if the amino acid sequences as recited included other residues on either end, or if the peptides are part of a fusion protein, and if so, what is the fusion partner.

12. Claims 32-37 are indefinite and ambiguous in the recitation of "at least a first detectable label". One skilled in the art could not determine if the peptides are to be labeled with one or more labels, and if more than one label, which ones.

13. Claims 44-45 are indefinite and ambiguous in the recitation of "at least a first immunostimulant" and "at least a first adjuvant". One skilled in the art could not determine if it is important to have more than one immunostimulant or adjuvant, if indeed immunostimulants and adjuvants are distinct entities since the specific examples recited in claim 45 refer back to both the immunostimulants and adjuvants, and if applicant wants a combination of immunostimulants or adjuvants, which combination.

14. Claim 47 is indefinite and ambiguous in the recitation of "at least a first detection reagent". One skilled in the art would not know how many labels were to be added to the peptide.

15. Claim 49 is indefinite and ambiguous in the recitation of "p33QIK or p63Krs1 peptide or polypeptide". It is unclear whether the peptide or polypeptide refers back solely to p63Krs1 or also to p33QIK.

16. Claims 51-52 are indefinite and ambiguous in the recitation of a kit comprising a peptide and at least one component for performing immunoprecipitation, a dot blot, an ELISA, an RIA, or a Western blot. The specification discloses on pages 21-24 immunoprecipitation, a dot blot, an ELISA, an RIA, or a Western blot, but does not disclose any of these assays in which a peptide of SEQ ID NO: 2 is used, only an antibody to detect the full-length protein in a sample. It is unclear what role the peptide has in the kit.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 33-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification and the claims as originally filed do not provide clear support for an isolated peptide wherein said at least a first label is a labelled secondary antibody that specifically binds to said peptide, said polypeptide, or said antibody (claim 33); wherein said radiolabel comprises 3H, 14C, 32P, 35S, 90Y, 99Tc, 125I, or 131I (claim 34), wherein said chromogenic label comprises alkaline phosphatase, peroxidase, beta-glucuronidase, beta-D-glucosidase, beta-D-galactosidase, urease, glucose oxidase/peroxidase, or galactose oxidase/peroxidase (claim 35); wherein said fluorescent label comprises a fluorescent protein, fluorescein, rhodamine, or auramine (claim 36); or wherein said fluorescent protein

comprises at least a first green fluorescent protein, or at least a first humanized green fluorescent protein (claim 37), and applicant's amendment, filed 1/23/2002 does not point to support for said labels in the specification.

19. Claims 1-8, 10-11, 32-37, and 42-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO: 2, a peptide consisting of residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76, said SEQ ID NO: 2/peptides in a pharmaceutically acceptable excipient to be used to generate antibodies which recognize non-human p33 to diagnose the therapeutic effectiveness of cancer treatments; and wherein the immune complexes (said peptides/polypeptide--antibody) can be detected indirectly with another labeled antibody; a kit comprising said peptides, does not reasonably provide enablement for any peptide/polypeptide comprising residues 1-322 of SEQ ID NO: 2, any peptide/polypeptide from 9 to about 20/30/40/50/60/70 amino acids in length comprising at least a first contiguous amino acid sequence according to any one of SEQ ID NOS: 3-76, and/or at least a second contiguous amino acid sequence according to any one of SEQ ID NOS: 3-76, any other labeled peptide/polypeptide thereof for detection, diagnostic, or therapeutic purposes, any nucleic acid encoding said peptides/polypeptide, or any antibody to said peptide/polypeptide in a pharmaceutically acceptable excipient to be used for in vivo therapy of any disease, or for diagnosis of the therapeutic effectiveness of any disease other than cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

(A) The claims as written encompass the genus of peptide and polypeptide amino acid sequences. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

Applicant discloses a single polypeptide comprising SEQ ID NO: 2 (491 residues), a peptide consisting of amino acid residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76 in the instant specification. Applicant has taught a polypeptide comprising SEQ ID NO: 2, peptides consisting of SEQ ID NOS: 3-76 and a peptide consisting of amino acid residues 1-322 of SEQ ID NO: 2. Applicant has not taught how many peptides are included in "at least a first" and "at least a second" contiguous amino acid sequence, nor has applicant disclosed if the peptides linked together are in the order of the natural amino acid sequence of SEQ ID NO: 2, or if they can be rearranged in a random order. Applicant has not taught how to make and/or use any isolated peptide from 9 to about 20/30/40/50/60/70 amino acids in length other than peptides consisting of SEQ ID NOS: 3-76. The structural and functional characteristics of said peptides are not defined in the claim. Further, applicant has not taught how to make or use any peptide as claimed labeled with a spin label, a radiolabel, a fluorogenic label, a chromogenic label, an chemiluminescent label, a fluorescent label, or any other type of label.

"Comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a peptide "comprising" from 9 to about 20/30/40/50/60/70 amino acids in length of SEQ ID NOS: 3-76 or amino acid residues 1-322 of SEQ ID NO: 2 includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 3-76 cannot support the entire genus of peptides from 9 to about 20/30/40/50/60/70 amino acids in length having SEQ ID NOS: 3-76 or amino acid residues 1-322 of SEQ ID NO: 2 as part of their sequence.

It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular).

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated amino acids from 9 to about 20/30/40/50/60/70 amino acids in length having "SEQ ID NOS: 3-76 or residues 1-322 of SEQ ID NO: 2" encompassed by the claimed invention other than "amino acids set forth by SEQ ID NO: 2" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. generation of antibodies which recognize p33) requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain functional aspects the peptides and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation.

In re Fisher, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of

experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention.

(B) With regard to **claims 44-46**, there is insufficient guidance and direction as to make and use SEQ ID NO: 2 (p33)-specific antibodies wherein the antibodies bind a peptide comprising from 9 to about 70 amino acids in length of SEQ ID NOS: 3-76, a peptide comprising residues 1-322 of SEQ ID NO: 2, or a fusion protein comprising "at least a first" and/or "at least a second" p33 peptide comprising from 9 to about 70 amino acids in length of SEQ ID NOS: 3-76 for *in vivo* therapeutic purposes.

The genus encompasses antibodies that can specifically bind polypeptides wherein such polypeptides have numerous differences in amino acid sequences at positions other than the length of residues 1-322 of SEQ ID NO: 2 or peptides from 9 to about 70 amino acids in length of SEQ ID NOS: 3-76, including numerous differences in linear and conformational epitopes; and further encompasses antibodies which are coupled with an unlimited number of polypeptides as fusion proteins.

However, the present specification fails to provide sufficient disclosure of such polypeptides that maintain the structural and functional properties of the p33 polypeptide set forth in SEQ ID NO: 2 wherein the other amino acids can vary. The specification does not provide sufficient guidance as to which of the amino acids may be changed while p33 polypeptide/peptide structural or functional activity and specificity is retained. Further, the specification fails to provide guidance as to the unlimited number of polypeptides which can be fusion partners for peptides comprising from 9 to about 70 amino acids in length of SEQ ID NOS: 3-76 and residues 1-322 of SEQ ID NO: 2.

Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teach single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Futher, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Additionally, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

Because of this lack of guidance, the extended experimentation that would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al.; in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other 499E9 polypeptides encompassed by the claimed invention.

The scope of the claimed p33-specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claimed invention. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and, in turn, nucleic acid sequence, and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins/nucleic acids and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed p33-specific antibodies in manner reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by the genus of polypeptides as recited in the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the amino acids and still maintain biological activity or structural specificity of p33 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant discloses on page 3, paragraph 2 that p33/p36 are activated in cancer cells following treatment with anti-cancer agents and that detection of protein activity with the antibody is a good therapeutic efficacy marker. Applicant further discloses on page 63, lines 17-18, and page 64, lines 10-12 that p33 activity is profound in cells undergoing apoptosis (i.e. cell death) and that elevated activity correlated with the induction of apoptosis. Finally, applicant discloses on page 6, paragraph 1, that preferred antibodies of the invention may be non-cross reactive with other polypeptides, including human polypeptides, or they may bind to non-human p33 or p63 polypeptides, but not to human p33 or p63; and page 5, lines 1-14 that said antibodies can alter, reduce, or inhibit the activity of p63 or p33.

Goyns et al. (Clin Oncol (R Coll Radiol) 1991 May;3(3):168-76) teach that cell proliferation is uncontrolled in cancer due to oncogenes. If, as applicant discloses, that p33 activity is increased following treatment with anti-cancer agents and that detection of protein activity with the antibody is a good therapeutic efficacy marker, the cancer cells expressing the increased p33 activity are dying. Therefore, it would not be beneficial to the patent suffering from cancer to use an antibody which binds p33 or a peptide of p33 to act as an antagonist of p33, because they could interfere with the cellular processes of apoptosis, and instead, enhance the uncontrolled cellular proliferation of the cancer cells, which is in direct contrast to the desired therapy. Indeed, enhancement of cancer cell growth is NOT a recognized therapy in the art.

Applicant has taught how to make and use SEQ ID NOS: 2-76 and residues 1-322 of SEQ ID NO: 2 to generate antibodies which bind to native p33 to serve as diagnostic markers of therapeutic efficacy of cancer treatments.

Applicant has not provided any working examples of peptides of p33 or antibodies generated against said peptides which are therapeutic with respect to cancer treatment. Applicant has not taught how to use any peptide of p33 or any antibody which binds to p33 as a therapeutic treatment regimen for patients suffering from cancer.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

20. Claims 1-8, 10-11, 32-37, and 42-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a polypeptide comprising SEQ ID NO: 2, a peptide consisting of residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76, said SEQ ID NO: 2/peptides in a pharmaceutically acceptable excipient to be used to generate antibodies which recognize non-human p33 to diagnose the therapeutic effectiveness of cancer treatments; and wherein the immune complexes (said peptides/polypeptide--antibody) can be detected indirectly with another labeled antibody; a kit comprising said peptides.

Applicant is not in possession of any peptide/polypeptide comprising residues 1-322 of SEQ ID NO: 2, any peptide/polypeptide from 9 to about 20/30/40/50/60/70 amino acids in length comprising at least a first contiguous amino acid sequence according to any one of SEQ ID NOS: 3-76, and/or at least a second contiguous amino acid sequence according to any one of SEQ ID NOS: 3-76, any other labeled peptide/polypeptide thereof for detection, diagnostic, or therapeutic purposes, any nucleic acid encoding said peptides/polypeptide, or any antibody to said peptide/polypeptide in a pharmaceutically acceptable excipient to be used for in vivo therapy of any disease, or for diagnosis of the therapeutic effectiveness of any disease other than cancer.

Conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). A description of a genus of polypeptide/peptide sequences may be achieved by means of a recitation of a representative number of polypeptides/peptides having SEQ ID NOS: 3-76, residues 1-322 of SEQ ID NO: 2, or at least a first peptide and at least a second peptide of SEQ ID NOS: 3-76, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

21. The filing date of the instant claims is deemed to be that of the instant application, 3/20/2001. Provisional application 60/193,550 does not provide support for a) a peptide comprising at least a first contiguous amino acid sequence, pharmaceutically acceptable excipient, immunostimulant, adjuvant, or detection reagent (claims 1, 7, 32-33, 37, 43-45, and 47), (b) at least a second contiguous amino acid sequence (claim 10), (c) a peptide consisting of a contiguous amino acid sequence (claim 9), (d) a polypeptide comprising, consisting essentially of, or consisting of amino acid residues 1-322 of SEQ ID NO: 2 (claims 11-12), (e) any peptide of any length comprising any label (claims 32-37 and 47-49), (f) any adjuvant (immunostimulant) other than CFA (claim 45), (g) formulation for parenteral, intranasal, transdermal, or oral administration (claim 45), or (h) a kit comprising any peptide or polypeptide (claim 50). Therefore, with respect to the prior art search, the claims will be examined according to the filing date of the instant application.

Claim Rejections - 35 USC § 102

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al. (PNAS 1996; 93: 10099-10104).

Taylor et al. teach two protein kinases, Krs-1 and Krs-2, and antibodies generated against said proteins (see the entire document, the Abstract, Materials on page 10100 in particular). Peptide sequences were generated from said proteins, and antibodies generated against the proteins to immunoprecipitate the Krs-1 and Krs-2 proteins (see page 10101, right column; and page 10102 in particular). The sequence of Krs-1 depicted in Figure 3 is 100% identical to SEQ ID NO: 2 disclosed in the instant application using the Smith-Waterman model. Therefore, the peptide used to generate the antibody was inherently in a pharmaceutical

composition. SEQ ID NO: 2 is a peptide "comprising SEQ ID NO: 5", "at least a first" contiguous amino acid sequence, and "at least a second" contiguous amino acid sequence.

"Consisting essentially of" is open-ended language and includes amino acid residues outside of the peptide sequence recited in the claims. Consequently, an isolated polypeptide "consisting essentially of" the amino acid sequence from position 1 to position 322 of SEQ ID NO: 2 reads on the reference intact polypeptide of SEQ ID NO: 2.

Therefore, the Taylor et al. reference anticipates the claimed invention.

24. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Creasy et al. (Gene, 1995; 167: 303-306).

Creasy et al. teach an amino acid and nucleic acid sequence that is 100% identical to SEQ ID NO: 2 disclosed in the instant application using the Smith-Waterman model.

"Consisting essentially of" is open-ended language and includes amino acid residues outside of the peptide sequence recited in the claims. Consequently, an isolated polypeptide "consisting essentially of" the amino acid sequence from position 1 to position 322 of SEQ ID NO: 2 reads on the intact polypeptide of SEQ ID NO: 2.

Therefore, the Creasy et al. reference anticipates the claimed invention.

25. Applicant is notified that SEQ ID NOS: 3-76 are free of the prior art.

26. Claim 12 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

27. No claim is allowed.

28. The drawings are objected to because of the errors listed on the PTO-948; therefore, the drawings fail to comply with 37 CFR 1.84.

The Patent and Trademark Office no longer makes drawing changes. See 1017 O.G. 4. It is applicant's responsibility to ensure that the drawings are corrected. Corrections must be made in accordance with the instructions below.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Patent Examiner
Technology Center 1600
February 25, 2002

Christina Chan

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